Sepsis-Induced Glomerular Endothelial Dysfunction Mediates Reductions in GFR and Increases in Protein Filtration

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Background: Sepsis is now the leading cause of acute kidney injury (AKI) known to decrease Glomerular filtration rate (GFR) and increase proteinuria. There also exists a discrepancy between renal perfusion and GFR.

Methods: To evaluate the potential role of the glomerulus in the overall pathogenesis of these abnormalities, we studied surface glomeruli in 8-10 week old Munich Wistar Fr Ömter rats using intravital 2-photon microscopy in a cecal ligation and puncture (CLP) model of sepsis to ask targeted questions and compare the metric of measured GFR to serum creatinine changes at 24 hours post CLP.

Results: Male rats undergoing CLP showed an increase in serum creatinine from 0.23 +/- 0.06 mg/dl to 0.80 +/-0.17 ($P \leq 0.01$) and a decrease in real time GFR from 0.69 +/- 0.06 ml/min/100gm body wt to 0.34 +/-0.15 ($P \leq 0.01$). Hemodynamic monitoring revealed normal and hyperdynamic cardiac status within the CLP group. Quantitative analysis of 15 glomeruli in three CLP septic rats revealed a reduction in red blood cell flow rates within capillary loops from 1,771 +/- 467 to 576 +/- 327 um/sec ($P \leq 0.01$); an increase in WBC adherence to glomerular capillary endothelial cells from 0.42 +/-0.33 to 7.25 +/- 5.82 WBC's/standardized glomerular volume ($P \leq 0.05$) in CLP rats; and an increase in the glomerular sieving coefficient (GSC) of a 150kD dextran from 0.007 +/- 0.003 to 0.097 +/- 0.046 ($P \leq 0.05$). Rouleaux formations were seen only in septic rats.

Conclusions: These data indicate glomerular endothelial-WBC interactions during sepsis, in part, explain the reduction in GFR and increased filtration of large molecular weight proteins. The results from real time GFR accurately detected the drop in renal function for this model of sepsis.